102. (New) A method for producing a polypeptide, the method comprising the steps of:

culturing a recombinant host cell containing the polynucleotide of claim 94 under conditions suitable for the expression of an encoded polypeptide;

recovering the polypeptide from the host cell culture.--

A10 cont'd

REMARKS

Formal Matters

Claims 13-102 are pending after entry of the amendments set forth herein.

Cancel claims 1-12 without prejudice with renewal, without intent to acquiesce to any rejection that may be applied thereon, and without the intent to abandon any subject matter encompassed therein.

New claims 13-102 are added.

Support for new claims 13-102 is found throughout the specification, including in the claims as originally filed. Support for claims directed to polynucleotides is found in the specification at, for example, page 2, line 24 to page 3, line 19; page 4, line 32 to page 5, line 18; page 5, line 34 to page 6 line 2; page 7, line 23 to page 8, line 16; page 16, lines 23 to page 17, line 12; and page 17, line 33 to page 18, line 14. Support for new claims directed to a method of producing a polypeptide using the recited polynucleotide is found in the specification at, for example, page 9, line 12 to page 10, line 4.

No new matter is added.

Restriction Requirement

In the Office Action dated December 19, 2000, the Examiner set forth a Restriction Requirement requiring election of one of five different groups of claims.

In response, applicants hereby elect to prosecute the claims of Group II, which includes claims drawn to isolated polynucleotides. Applicants expressly reserve the right under 35 USC §121 to file a divisional application directed to the non-elected subject matter during the pendency of this application.

The claims presented in this amendment are directed to the subject matter of Group II, and further include claims for methods of using the recited polynucleotides. Applicants respectfully submit that such claims directed to methods of use of the polynucleotides can be properly examined with the subject matter of the elected group.

The Office Action further stated that if Group II is elected, then applicants must indicate whether the elected sequence do or do not comprise an open reading frame, and then must further elect: a) a single nucleic acid sequence, if the nucleic acid sequence comprises an open reading frame; or 2) up to 10 nucleic acid sequences if the nucleic acid does not comprise an open reading frame. Applicants respectfully traverse this aspect of the Restriction Requirement.

Applicants respectfully traverse the Restriction Requirement on the grounds that MPEP §803.04 provides for examination of a reasonable number of nucleotide sequences to be claimed in a single application (see MPEP §2434, which states that the Commissioner has partially waived the requirements of 37 CFR §1.141 for this purpose). Under this policy, in most cases, up to 10 independent and distinct nucleotide sequences will be examined in a single application without restriction. The relevant language from this section of the MPEP is provided below for convenience:

> Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq. Nevertheless, to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided sua sponte to partially waive the requirements of 37 CFR 1.141 et seq. and permit a reasonable number of such nucleotide sequences to be claimed in a single application. See Examination of Patent Applications Containing Nucleotide Sequences, 1192 O.G. 68 (November 19, 1996).
>
> It has been determined that normally ten sequences constitute a reasonable number for examination purposes. Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction. In addition to the specifically selected sequences, those sequences which are patentably indistinct from the selected sequences will also be examined. Furthermore, nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together.

> In some exceptional cases, the complex nature of the claimed material, for example a protein amino acid sequence reciting three dimensional folds, may necessitate that the reasonable number of sequences to be selected be less than ten. In other cases, applicants may petition pursuant to 37 CFR 1.181 for examination of additional nucleotide sequences by providing evidence that the different nucleotide sequences do not cover independent and distinct inventions.

MPEP§ 803.04. Emphasis added.

Applicants do not read this section of the MPEP to contain a specific requirement for either indicating whether the elected sequence contains an open reading frame, and, if so, to elect only a single sequence. To the contrary, the language of the MPEP suggests that even where the sequences encode for different proteins, up to ten sequences can still be examined together.

Therefore, the Examiner is respectfully requested to withdraw this requirement.

Conclusion

If the Examiner believes a teleconference would expedite prosecution, he is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: March 19, 2001

By: _____
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F:\DOCUMENT\2300\1492\rsp rest reqmt (12-19-00) 2300-1492.doc

VERSION WITH MARKINGS TO SHOW CHANGES MADE

*****Inserted text is indicated by **bold and underlined** text. Deleted text is indicated by brackets.*****

Paragraph at page 11, lines 8-26 has been amended as follows:

Query and individual sequences can be aligned using the methods and computer programs described above, and include BLAST 2.0 [, available over the world wide web at http://www.ncbi.nlm.nih.gov/BLAST/] **(National Center for Biotechnology Information, Bethesda, Maryland)**. See also Altschul, et al. *Nucleic Acids Res.* (1997) *25*:3389-3402. Another alignment algorithm is Fasta, available in the Genetics Computing Group (GCG) package, Madison, Wisconsin, USA, a wholly owned subsidiary of Oxford Molecular Group, Inc. Other techniques for alignment are described in Doolittle, *supra*. Preferably, an alignment program that permits gaps in the sequence is utilized to align the sequences. The Smith-Waterman is one type of algorithm that permits gaps in sequence alignments. See *Meth. Mol. Biol.* (1997) *70*: 173-187. Also, the GAP program using the Needleman and Wunsch alignment method can be utilized to align sequences. An alternative search strategy uses MPSRCH software, which runs on a MASPAR computer. MPSRCH uses a Smith-Waterman algorithm to score sequences on a massively parallel computer. This approach improves ability to identify sequences that are distantly related matches, and is especially tolerant of small gaps and nucleotide sequence errors. Amino acid sequences encoded by the provided polynucleotides can be used to search both protein and DNA databases. Incorporated herein by reference are all sequences that have been made public as of the filing date of this application by any of the DNA or protein sequence databases, including the patent databases (*e.g.*, GeneSeq). Also incorporated by reference are those sequences that have been submitted to these databases as of the filing date of the present application but not made public until after the filing date of the present application.

Paragraph at page 14, lines 9-20 has been amended as follows:

Profiles can **be** designed manually by (1) creating an MSA, which is an alignment of the amino acid sequence of members that belong to the family and (2) constructing a statistical representation of the alignment. Such methods are described, for example, in Birney *et al.*, *Nucl. Acid Res.* (1996)

24(14): 2730-2739. MSAs of some protein families and motifs are publicly available. For example, [http://genome.wustl.edu/Pfam/] **the Pfam database available from Washington University (St. Louis, Missouri)** includes MSAs of 547 different families and motifs. These MSAs are described also in Sonnhammer *et al.*, *Proteins* (1997) *28*: 405-420. [Other sources over the world wide web include the site at http://www.embl-heidelberg.de/argos/ali/ali.html; alternatively, a message can be sent to ALI@EMBL-HEIDELBERG.DE for the information.] **Other publicly available sources include those over the world wide web provided by the European Molecular Biology Laboratory (Heidelberg, Germany).** A brief description of these MSAs is reported in Pascarella *et al.*, *Prot. Eng.* (1996) *9(3)*:249-251. Techniques for building profiles from MSAs are described in Sonnhammer *et al.*, *supra*; Birney *et al.*, *supra*; and "Computer Methods for Macromolecular Sequence Analysis," *Methods in Enzymology* (1996) *266*, Doolittle, Academic Press, Inc., San Diego, California, USA.

Paragraph beginning on page 24, line 18 has been amended as follows:

Mapping. Polynucleotides of the present invention can be used to identify a chromosome on which the corresponding gene resides. Such mapping can be useful in identifying the function of the polynucleotide-related gene by its proximity to other genes with known function. Function can also be assigned to the polynucleotide-related gene when particular syndromes or diseases map to the same chromosome. For example, use of polynucleotide probes in identification and quantification of nucleic acid sequence aberrations is described in USPN 5,783,387. An exemplary mapping method is fluorescence in situ hybridization (FISH), which facilitates comparative genomic hybridization to allow total genome assessment of changes in relative copy number of DNA sequences (see, e.g., Valdes *et al.*, *Methods in Molecular Biology* (1997) *68*:1). Polynucleotides can also be mapped to particular chromosomes using, for example, radiation hybrids or chromosome-specific hybrid panels. See Leach *et al.*, *Advances in Genetics*, (1995) *33*:63-99; Walter *et al.*, *Nature Genetics* (1994) *7*:22; Walter and Goodfellow, *Trends in Genetics* (1992) *9*:352. Panels for radiation hybrid mapping are available from Research Genetics, Inc., Huntsville, Alabama, USA. Databases for markers using various panels are publicly available via the world wide web [at http:/F/shgc-www.stanford.edu; and http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl] **from the Stanford Genome Center and The Whitehead Institute for Biomedical Research/MIT Center for Genome Research**. The

statistical program RHMAP can be used to construct a map based on the data from radiation hybridization with a measure of the relative likelihood of one order versus another. RHMAP is available [via the world wide web at http://www.sph.umich.edu/group/statgen/software] **from the University of Michigan, Center for Statistical Genetics, Ann Arbor, Michigan**. In addition, commercial programs are available for identifying regions of chromosomes commonly associated with disease, such as cancer.

Paragraph at page 46, lines 26-33 has been amended as follows:

SEQ ID NOS:1-1079 were translated in all three reading frames, and the nucleotide sequences and translated amino acid sequences used as query sequences to search for homologous sequences in either the GenBank (nucleotide sequences) or Non-Redundant Protein (amino acid sequences) databases. Query and individual sequences were aligned using the BLAST 2.0 programs [, available over the world wide web at http://ww.ncbi.nlm.nih.gov/BLAST/] **(National Center for Biotechnology Information, Bethesda, Maryland)**. (see also Altschul, et al. *Nucleic Acids Res.* (1997) *25*:3389-3402). The sequences were masked to various extents to prevent searching of repetitive sequences or poly-A sequences, using the XBLAST program for masking low complexity as described above in Example 1.

Paragraph at page 48, lines 25-34 has been amended as follows:

Some polynucleotides exhibited multiple profile hits where the query sequence contains overlapping profile regions, and/or where the sequence contains two different functional domains. Each of the profile hits of Table 3 are described in more detail below. The acronyms for the profiles (provided in parentheses) are those used to identify the profile in the Pfam and Prosite databases. The Pfam database can be accessed through [any of the following URLS: http://pfam.wustl.edu/index.html; http://www.sanger.ac.uk/ Software/Pfam/; and http://www.cgr.ki.se/Pfam/. The Prosite database can be accessed at http://www.expasy.ch/prosite/.] **web sites supported by the Washington University, St. Louis (Missouri), The Sanger Centre (United Kingdom); and The Karolinska Institute Center for Genomics Research. The Prosite database is publicly available through the ExPASy Molecular Biology Server.** The public

information available on the Pfam and Prosite databases regarding the various profiles, including but not limited to the activities, function, and consensus sequences of various proteins families and protein domains, is incorporated herein by reference.

Paragraph at page 49, lines 25-35 has been amended as follows:

ATPases Associated with Various Cellular Activities (ATPases; Pfam Accession No. PF0004). SEQ ID NOS:1035, 1058, and 1072 corresond to a sequence that encodes a member of a family of ATPases Associated with diverse cellular Activities (AAA). The AAA protein family is composed of a large number of ATPases that share a conserved region of about 220 amino acids containing an ATP-binding site (Froehlich *et al., J. Cell Biol.* (1991) *114*:443; Erdmann *et al. Cell* (1991) *64*:499; Peters *et al., EMBO J.* (1990) *9*:1757; Kunau *et al., Biochimie* (1993) *75*:209-224; Confalonieri *et al., BioEssays* (1995) *17*:639; [http://yeamob.pci. chemie.uni-tuebingen.de/AAA/Description.html] **see also the AAA Server Homepage**). The AAA domain, which can be present in one or two copies, acts as an ATP-dependent protein clamp (Confalonieri *et al.* (1995) *BioEssays 17*:639) and contains a highly conserved region located in the central part of the domain. The consensus pattern is: [LIVMT]-x-[LIVMT]-[LIVMF]-x-[GATMC]-[ST]-[NS]-x(4)-[LIVM]- D-x-A-[LIFA]-x-R.

Paragraph at page 51, lines 19-33 has been amended as follows:

Helicases conserved C-terminal domain (helicase_C; Pfam Accession No. PF00271). SEQ ID NOS:227 and 1058 represent polynucleotides encoding novel members of the DEAD/H helicase family. The DEAD box family comprises a number of eukaryotic and prokaryotic proteins involved in ATP-dependent, nucleic-acid unwinding. All DEAD box family members of the above proteins share a number of conserved sequence motifs, some of which are specific to the DEAD family while others are shared by other ATP-binding proteins or by proteins belonging to the helicases 'superfamily' (Hodgman, *Nature* (1988) *333*:22 and *Nature* (1988) *333*:578[; http://www.expasy.ch/www/linder/ HELICASES_TEXT.html)]. One of these motifs, called the 'D-E-A-D-box', represents a special version of the B motif of ATP-binding proteins. Some other proteins belong to a subfamily which have His instead of the second Asp and are thus said to be 'D-E-A-H-box' proteins (Wassarman D.A., et al., *Nature* (1991) *349*:463; Harosh I., et al., *Nucleic Acids*

Res. (1991) *19*:6331; Koonin E.V., et al., *J. Gen. Virol.* (1992) *73*:989[; http://www.expasy.ch/www/linder/ HELICASES_TEXT.html)]. The following signature patterns are used to identify member for both subfamilies: 1) [LIVMF](2)-D-E-A-D-[RKEN]-x-[LIVMFYGSTN]; and 2) [GSAH]-x-[LIVMF](3)-D-E-[ALIV]-H-[NECR].

Paragraph beginning at page 55, line 32 has been amended as follows:

WW/rsp5/WWP domain signature and profile (WW domain; Pfam Accession No. PF00397). SEQ ID NO:606 corresponds to a gene encoding a protein comprising a WW domain. The WW domain (Bork *et al. Trends Biochem. Sci.* (1994) *19*:531-533; Andre *et al. Biochem. Biophys. Res. Commun.* (1994) *205*:1201-1205; Hofmann *et al. FEBS Lett.* (1995) *358*:153-157; Sudol *et al. FEBS Lett.* (1995) *369*:67-71[; http://www.bork.embl-heidelberg.de/Modules/ww-gif.html)] (also known as rsp5 or WWP) was discovered as a short conserved region in a number of unrelated proteins, among them dystrophin, the gene responsible for Duchenne muscular dystrophy. The domain, which spans about 35 residues, is repeated up to 4 times in some proteins. It has been shown (Chen *et al. Proc. Natl. Acad. Sci. U.S.A.* (1995) *92*:7819-7823) to bind proteins with particular proline-motifs, [AP]-P-P-[AP]-Y, and thus resembles somewhat SH3 domains. The WW domain conatins beta-strands grouped around four conserved aromatic positions, generally tryptophan. The name WW or WWP derives from the presence of two tryptophane as well as a conserved proline. The WW domain is frequently associated with other domains typical for

Table 12 on page 65, lines 15-16 has been amended as follows:

Table 12: Pools of Clones and Libraries Deposited with ATCC on or before September 23, 1999

Library No.	CMCC No.	ATCC Deposit No.	Library No.	CMCC No.	ATCC Deposit No.
ES55	5058	**PTA-739**	ES65	5068	**PTA-749**
ES56	5059	**PTA-740**	ES66	5069	**PTA-750**
ES57	5060	**PTA-741**	ES67	5070	**PTA-751**
ES58	5061	**PTA-742**	ES68	5071	**PTA-752**
ES59	5062	**PTA-743**	ES69	5072	**PTA-753**
ES60	5063	**PTA-744**	ES70	5073	**PTA-754**
ES61	5064	**PTA-745**	ES71	5074	**PTA-755**
ES62	5065	**PTA-746**	ES72	5075	**PTA-756**
ES63	5066	**PTA-747**	ES73	5076	**PTA-757**
ES64	5067	**PTA-748**	ES74	5077	**PTA-758**

(6510-223 cont)

could not find file but looked @ patent (nothing unusual found)

Future 223 Applications

After reviewing the file history for 223 (except 223 DIV), I found the following uses which had been disclosed but not claimed in the previous applications.

1a. Therapeutic compositions may be used to inhibit the migration of cells, i.e. cancer and autoimmune situations, have an increased number of collagen receptors, which can be blocked by the peptides.

1b. Drug delivery to infected T-cells with potential applications in AIDS therapy.

1c. In arthritis, T-cells aggregate. Injection of peptides should help. How?

Below is the complete reference for T-cells in the 223 patent history.
From CIP and CIP2.

"While composites of the invention are typically used in applications (both in the body and outside the body) for growing or promoting the growth of cells, another embodiment of this invention is to inhibit the migration of cells. For example, cells that are out of normal regulation processes (e.g., cancer and autoimmune situations) have an increased number of collagen receptors, which can be blocked by the inventive synthetic peptides due to competitive (and inhibitory) binding with respect to collagen. This aspect of the invention is illustrated by the following T-cell studies. Other implications for the T-cell aspects of this invention include drug delivery to infected T-cells with potential applications in AIDS therapy.

EXAMPLE 7

The interactions of T-lymphocytes with the extracellular matrix play an important role in their differentiation, maturation, and migration. Collagen is a major component of the physiological milieu in which T-cells reside, such as by affecting differentiation and migration behavior.

Mixed populations of peripheral blood CD4 and CD8 lymphocytes showed a strong affinity for substrates coated with rat tail type I collagen. Cultured T-cells were incubated in collagen-coated dishes in serum free medium, in the presence and absence of inventive peptides. The interactions between T-cells and collagen was markedly inhibited by inventive peptides (SEQ ID NOS. 1, 2, and 3). The maximal rate of T-cell binding was observed in the first 30 minutes in the absence of the inventive peptides. Inhibition was examined at several concentrations and times. Maximal inhibition by the peptides occurred at 30 minutes at 37□C at a concentration of 35 μM.

Thus, the molecular site on type I collagen involved in the interaction with T-cells appears to be the same as involved in fibroblast binding."

(paragraph only in CIP2) "P-15 also induces metalloproteinases in dermal fibroblasts. This activity is useful for resolving fibrosis. In composites with hydroxyapatite, P-15 causes osteodifferentiation in non-osteoblastic (dermal) fibroblasts. This is confirmed by the induction of the following genes: type I collagen, collagenase, alkaline phosphatase, osteonectin, transforming growth factor β (TGF-β), and osteogenin (bone morphogenic protein, BMP-7). These studies confirm that the inventive peptides mimic the biological activity of collagen by binding to specific receptors and inducing biochemical processes characteristic of those induced by collagen itself.

In conditions such as arthritis, T-cells aggregate. Administration (such as by injection at the affected site) of the inventive peptides in a physiologically acceptable solution should prove efficacious. Administration (intravenous, intradermal, or subcutaneous) in amounts from about 1 to about 200 μK/kg body weight in combination with a pharmaceutically acceptable carrier, such as isotonic saline phosphate buffer solution or the like, should prove therapeutically useful. Pharmaceutically acceptable salts of the inventive peptides with organic and inorganic acids can be formed.

It is to be understood that while the invention has been described above in conjunction with preferred specific embodiments, the description and examples are intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims."

2. Uses in fibrosis.

CIP2 mentions information on P-15 inducing metalloproteinases in dermal fibroblasts and this activity is useful in fibrosis.

From CIP2- "P-15 also induces metalloproteinases in dermal fibroblasts. This activity is useful for resolving fibrosis. In composites with hydroxyapatite, P-15 causes osteodifferentiation in non-osteoblastic (dermal) fibroblasts. This is confirmed by the induction of the following genes: type I collagen, collagenase, alkaline phosphatase, osteonectin, transforming growth factor β (TGF-β), and osteogenin (bone morphogenic protein, BMP-7). These studies confirm that the inventive peptides mimic the biological activity of collagen by binding to specific receptors and inducing biochemical processes characteristic of those induced by collagen itself."

3. Produce mAbs specific for the peptides for anti-idiotypic Abs for functional P-15 analogs.

From CIP---" In yet another embodiment, monoclonal antibodies may be raised against an epitopic region defined by P-15 or a portion thereof, or by any of the compounds of the present invention, wherein the epitopic region is responsible for binding and biological activity. By then raising antibodies against the first antibody, the binding region of the anti-idiotypic antibodies may provide functional analogs of P-15, or a functionally similar compound."

One use that came to mind was to use the peptides in organotypic raft cultures instead of rat tail collagen type I. Organotypic raft cultures are used when a cell differeniation is needed to produce skin for burn victims or for production of infectious virsus such as human papilloma viruses (HPV). Rat tail collagen is used a part of the support to grow cell cultures at a liquid/air interface to achieve cellular differentiation. The 233 specification supports the binding of cells to P-15 for cell prolifeaction.

> CIP3, example 6, relates to the peptides being utilized in a bioreactors. This patent mentions 3-D templates containing ligands for ECM receptors. It also describes the use of collagen fibers not the peptides. The matrices of the invention will promote the expansion of cell populations in a differentiated state. Matrices can be engineered like a normal bioreactor (not like a organotypic raft). Cells proliferate while submerged in medium (doesn't mention liquid/air interface). Doesn't list raft cultures. CIP3 indicates that bioreactors are used for the production of Abs. This patent also describes a bioreactor as packing material is porous inert expanded Teflon tubes. Hollow glass microshperes etc.

I think there is enough difference between CIP3 and in the raft culture idea for and application.

I hope this information helps in choosing a new 223 application.

510-223 Series (UC 89-241 Series)

6510-223US1
UC 89-241-1
07/393,621
filed Aug. 14, 1989
(abandoned)

6510-223WO1
UC 89-241-2 **(PCT)**?
US90/04538
filed Aug. 13, 1990
National Phase
WO 91/02537
pub. March 7, 1991

AT, BE, CH, DE, DK, ES, FR, GB, IT, JP, LU, NL, SE

A periodontal repair composition comprising peptides, the domain of which mimic collagen binding to cells and have enhanced binding relative to collagen,coated on hydroxylapatite particles.

6510-223CIP
UC 89-241-2
07/804,782
filed Dec. 9, 1991
U.S. Patent 5,354,736
issued Oct. 11, 1994

6510-223WO2
UC 89-241-2 **(PCT)**
US92/10420
filed Dec. 3, 1992
National Phase
WO 93/11781
pub. June 24, 1993

AT, BE, CA, CH, DE, DK, ES, FR, GB, GR, IE, IT, JP, LU, MC, NL, PT, SE

An implant comprising a matrix of polymer fibers (includes hydrogel) and a peptide, having a domain which mimics collagen binding to cells and has enhanced binding relative to collagen, bound to the matrix.

6510-223CIP2
UC 89-241-3
08/278,878
filed July 22, 1994
U.S. Patent 5,635,482
issued June 3, 1997

6510-223CIP3
UC 89-241-4
08/285,570
filed Aug. 3, 1994
U.S. Patent 5,674,848
issued Oct. 7, 1997

A packing material used for bioreactor cell culture comprising a matrix of polymer fiber beads (includes hydrogel) and a peptide, having a domain which mimics collagen binding to cells and has enhanced binding relative to collagen, bound to the matrix.

An apparatus for [soft tissue repair], [cartilage, tendon, or ligament repair], and [bone repair] comprising a structure of fibers (includes hydrogel), having interstices or pores and a compound present in an amount capable of promoting cell attachment to structure and its interstices/pores. The compound carried on structure has domain which mimics collagen binding to cells and has enhanced binding relative to collagen. An additive useful with medical repair or reconstructive apparatus which includes a peptide of aforementioned properties (refer to CIP).

6510-223DIV
UC 89-241-5
08/859,610
filed May 20, 1997
U.S. Patent 5,958,428
issued Sept. 28, 1999

6510-223CON
UC 89-241-6
09/328,347
filed June, 8, 1999
pending

A synthetic peptide having biological activity functionally comparable to peptide of sequence No. 1 (common to all cases in tree). An implant apparatus comprising a structure (which includes a ceramic, metal, polymer, or a metal-ceramic composite) having interstices/pores and a compound (having a domain that mimics collagen binding to cells) & living cells growing on the structure. A bone repair apparatus comprising a compatible structure including a ceramic, a compound of aforementioned properties and living cells derived from fibroblasts carried on the structure.